

**REMARKS**

In the present Amendment, claims 1, 6-11 and 14-17 have been cancelled without prejudice or disclaimer. Claim 2 has been rewritten into independent form and to improve its form. Claim 12 has been amended in view of the amendment to claim 2. Support for the amendment is found, for example, in the last paragraph at page 11 of the specification. Claims 18 and 19 have been amended to depend from claim 2. Claims 20 and 21 have been amended to recite a positive step and to depend from claim 2. Support for the amendments is found, for example, in the first paragraph at page 15 and at page 15, line 19 to page 16, line 14 of the specification. No new matter has been added, and entry of the Amendment is respectfully requested.

Upon entry of the Amendment, claims 2-5, 12, 13 and 18-21 will be pending.

1. At page 2 of the Action, claims 1-11, 18 and 19 are rejected under 35 U.S.C. § 102(b) as being anticipated by Takayanagi (US 5,945,564).

Takayanagi is cited as teaching 2,2-dideutero-5-aminolevulinic acid salts including the nitrate, phosphate, methanesulfonate and toluenesulfonate salts and both solid and liquid dosage forms as contrast media (abstract and col. 2, lines 49-65).

2. At page 2 of the Action, claims 1-7, 19 and 21 are rejected under 35 U.S.C. § 102(b) as being anticipated by Yoshida et al (US 5,489,572).

Yoshida et al. is cited as teaching 5-aminolevulinic acid (ALA) and salts including the nitrate and phosphate salts and both solid and liquid fertilizer forms (col. 2, lines 59-64).

3. At page 2 of the Action, claims 1-7, 19 and 21 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kuramochi et al (US 5,661,111).

Kuramochi et al is cited as teaching 5-aminolevulinic acid and salts including the nitrate and phosphate salts and both solid and liquid fertilizer forms (col. 2, lines 50-59).

4. At page 3 of the Action, claims 1-7, 19 and 21 are rejected under 35 U.S.C. § 102(b) as being anticipated by Tanaka et al (US 5,298,482).

Tanaka et al is cited as teaching 5-aminolevulinic acid and salts including the nitrate and phosphate salts and both solid and liquid fertilizer forms (col. 2, lines 19-25).

5. At page 3 of the Action, claims 12-17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Daisuke et al (JP 5310657), taken with Takayanagi, Kuramochi et al, and Tanaka et al.

Daisuke et al is cited as teaching eluting amino acids that are bound to cation exchange resin with aqueous ammonia.

Applicants submit that all the above rejections should be withdrawn because the cited references do not disclose or render obvious the present claimed invention, either alone or in combination.

The present claims have been amended to limit to recite that the ALA salt is the phosphate salt.

**Takayanagi**, while mentioning phosphates of (dideutero)ALA at col. 2, line 61, does not disclose any workable process for actually manufacturing the specific ALA phosphates of formula (I) of present claim 2.

As one allegedly suitable reaction, the acidic hydrolysis of compound (C) shown in the reaction scheme at col. 3 of Takayanagi is disclosed at col. 4, lines 26-32. However, as can be inferred from the disclosure therein, the acid to be used in this acidic hydrolysis must be a strong acid, such as HCl, HBr or a strong organic acid such as methane- or p-toluene sulfonic acid.

Thus, it is clear to one skilled in the art that this acidic hydrolysis cannot be performed with a weak acid such as phosphoric acid to obtain the presently claimed phosphate salt.

A second method for making the compound (I) of Takayanagi is shown in the reaction scheme at cols. 4-5. However, it can be seen that for making compound (I) from compound (H) in this reaction very vigorous reaction conditions are required, and it is clear to one skilled in the art that phosphoric acid would not be a suitable reactant in this reaction (col. 6, lines 46-57). Also, it is noted that from this reaction only compounds are obtained where the ALA derivative does not have a free carboxylic acid group, but rather a carboxyl group esterified by a group R<sup>1</sup>. Therefore, this process does not provide a suitable or workable way to obtain the presently claimed phosphate salt.

In view of the above, Takayanagi does not provide an enabling disclosure for making the presently claimed phosphate compounds, and therefore cannot stand against the novelty of the present claims.

**Yoshida et al, Kuramochi et al and Tanaka et al** do not teach any process as to how to make ALA phosphates. Although these references mention ALA phosphate, they do not provide any enabling disclosure for making the presently claimed phosphate compounds. Furthermore, no process is disclosed in these references according to which the presently claimed phosphate compounds could be obtained.

Therefore, the present claims are novel over Yoshida et al, Kuramochi et al and Tanaka et al.

Further, as shown by the attached articles, “Chemical instability of 5-aminolevulinic acid used in the fluorescence diagnosis of bladder tumors” (Journal of Photochemistry and

photobiology B: Biology 34 (1996) 143-148), ALA is unstable and it is very difficult to manufacture the ALA phosphate salt.

Still further, Applicants have searched “pentanoic acid, 5-amino-4-oxo-, phosphate (1:1) (5-aminolevulinic acid phosphate)” in the Data Base of CAS (Chemical Abstracts Service: <http://www.cas.org/>), and as a result, Applicants were able to confirm that the 5-aminolevulinic acid phosphate (ALA phosphate) was, for the first time, registered as No. 868074-65-1 on November 15, 2005. A copy of the search result is submitted herewith.

This is evidence that 5-aminolevulinic acid phosphate alone was not isolated and purified prior to March 28, 2005, the international filing date of the present application. The four documents cited in the search result are all patent applications by the present assignee, Cosmo Oil Co. Ltd.

That is, 5-aminolevulinic acid phosphate alone was isolated and purified for the first time by the present inventors.

Therefore, the present claims are not anticipated by and are patentable over Takayanagi, Yoshida et al, Kuramochi et al and Tanaka et al.

Additionally, as can be seen from the examples of the present specification, particularly from Examples 3-6 and Comparative Examples 1-3 at pages 18-21, the presently claimed ALA phosphates show a reduced smell and improved organoleptic properties as compared with the ALA•HC1 known in the art, even when ALA•HC1 was produced according to the same procedure as disclosed in the present specification (using hydrochloric acid instead of the phosphoric acid of formula (III)).

This is a significant improvement in product quality, especially in the field of medical compositions, where a patient can be repulsed by an unpleasant smell and/or taste of a medical

composition. Thus, improving the smell and taste of medical compositions providing ALA to a patient for therapeutic or diagnostic purposes improves the patient's compliance and thus gives a product of a higher quality. This improvement achieved by the present invention could not be foreseen by one skilled in the art based on the teachings of the cited prior art, and thus is unexpected.

Therefore, the present claims are not made obvious over and are patentable over the cited references.

In view of the above, reconsideration and withdrawal of all the §§102(b)/103(a) rejections based on the cited references are respectfully requested.

At page 4 of the Action, claim 20 is objected to as being dependent upon a rejected base claim, but is indicated to be allowable if rewritten in independent form.

Claim 20 is patentable in its present form because claim 2, from which claim 20 depends from, is patentable as discussed above.

Allowance is respectfully requested. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,


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Date: June 23, 2010

  
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